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1FW AF/1642

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of: Lioubin *et al.*	Confirmation No: 1603
Serial No.: 10/056,790	Group Art Unit: 1642
Filed: 1/23/2002	Examiner: Yaen, Christopher H.
For: RRP SEQUENCES AND KNOCKOUT MICE AND USES THEREOF	Attorney Docket No: EX02-004C

PETITION TO ENTER AMENDMENT UNDER 37 C.F.R. § 1.181

Director of Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Director:

This is a petition to enter an amendment filed on 2/25/2004 in the above referenced application, which was not entered by the examiner in the Final office action mailed 03/22/2004. Accompanying this petition are copies of the relevant actions and responses in the case, including the response concurrently filed with this petition. This petition is being filed within the first two months after the office action of 3/22/2004, making this a timely petition. No fees are believed to be due for the filing of this petition. However, if this belief is in error, the Director is authorized to charge any fees required for consideration of this paper and any other papers filed herewith to deposit account number 50-1108.

Statements Of Facts

A first office action on this application was filed on 8/1/2003.

Applicants' response addressing the issues was filed on 10/27/03.

The second, final office action was filed on 1/9/2004. This office action contained new grounds for rejection that could have been raised in the first office action but was not. This was brought to the attention of the examiner in a telephone

conversation on 2/19/2004 between the undersigned and the examiner. After a consultation with a supervisory examiner, the examiner informed the undersigned that the final rejection was premature, and the finality would be removed in the subsequent office action. Thereafter the applicants prepared and filed a complete after final response, filed on 2/25/2004, adopting examiner's suggestions, and removing any issues for rejection. Details of the conversation between the undersigned and the examiner were also highlighted in the response.

On 3/22/04, another final rejection was mailed, as a supplemental detailed action, on the merits of the application, in response to the amendment of 10/27/03. The action mailed on 1/9/04 was withdrawn in favor of the supplemental action. Further, the after-final amendments filed 2/25/2004 were not entered because they failed to comply with requirements of form expressly set forth in a previous office action. The rest of the office action resembles the office action of 1/9/04 very closely. Applicants are surprised and disappointed by the final rejection o f 3/22/04, not because it is another final rejection, but because the applicant's amendments were not entered. Further, the reasons stated in the 3/22/04 office action for not entering the amendment of 2/25/04 are not acceptable to the applicants, because the amendments adopted all suggestions of the examiner. Applicants are trying to promote, and follow, a fair patent prosecution procedure. It does not appear that proper procedure was followed by the examiner in this case. Applicants respectfully request the Director to review and enter the 2/25/2004 amendment.

Respectfully submitted,

Dated: May 3, 2004

Laleh Shayesteh Reg. No. 47,937

EXELIXIS, INC.
170 Harbor Way, P.O. Box 511
South San Francisco, California 94083-0511
Telephone: (650) 837-8223
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PTO/SB/21 (02-04)
Approved for use through 07/31/2006. OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Application Number	10/056,790
Filing Date	1/23/2002
First Named Inventor	Lioubin
Art Unit	1642
Examiner Name	Yaen, Christopher H.
Total Number of Pages in This Submission: 42	Attorney Docket Number

ENCLOSURES ***(check all that apply)***

- ☐ Fee Transmittal Form
  - ☐ Fee Attached
- ☐ Amendment / Reply
  - ☐ After Final
  - ☐ Affidavits/declaration(s)
- ☐ Extension of Time Request
- ☐ Express Abandonment Request
- ☐ Information Disclosure Statement
- ☐ Certified Copy of Priority Document(s)
- ☐ Response to Missing Parts/ Incomplete Application
  - ☐ Response to Missing Parts under 37 CFR 1.52 or 1.53
- ☐ Drawing(s)
- ☐ Licensing-related Papers
- ☒ Petition
- ☐ Petition to Convert to a Provisional Application
- ☐ Power of Attorney, Revocation Change of Correspondence Address
- ☐ Terminal Disclaimer
- ☐ Request for Refund
- ☐ CD, Number of CD(s) ____
- ☐ After Allowance Communication to Group
- ☐ Appeal Communication to Board of Appeals and Interferences
- ☐ Appeal Communication to Group **(Appeal Notice, Brief, Reply Brief)**
- ☐ Proprietary Information
- ☐ Status Letter
- ☒ Other Enclosure(s) *(please identify below)*:
  return receipt postcard

Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm *or* Individual name	Laleh Shayesteh, Reg. No. 47,937
Signature	
Date	May 3, 2004

CERTIFICATE OF TRANSMISSION/MAILING

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Typed or printed name	Shannon Paladini		
Signature	Shannon Paladini	Date	May 3, 2004

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REPLY TO FINAL REJECTION UNDER 37 C.F.R. § 1.116 (5p)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of: Lioubin *et al.*	Confirmation No: 1603
Serial No.: 10/056,790	Group Art Unit: 1642
Filed: 1/23/2002	Examiner: Yaen, Christopher H.
For: RRP SEQUENCES AND KNOCKOUT MICE AND USES THEREOF	Attorney Docket No: EX02-004C

REPLY TO FINAL REJECTION UNDER 37 C.F.R. § 1.116

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Via Facsimile (703) 872-9306

Dear Commissioner:

This is responsive to the office action mailed 03/22/2004, making this a timely response. No fees are believed to be due at this time. However, if this belief is in error, the Commissioner is authorized to charge any fees required for consideration of this paper and any other papers filed herewith to deposit account number 50-1108.

REMARKS

There are no further amendments to the claims in this case. Appendix A is a reiteration of the claim amendments presented in the amendment of 2/25/2004, which were not entered into the case.

It is believed that proper procedure has not been followed by the examiner for the prosecution of this application for the reasons set forth below. Applicants are trying to promote a fair prosecution of their application, and have followed all the proper procedures in this case. Accordingly, applicants request the examiner reconsider the non-entry of the 2/25/04 amendment. Accompanying this response is also a petition to enter the amendment of 2/25/2004 under 37 C.F.R.§ 1.181.

In the telephone conversation of February 19, 2004 between the undersigned and the examiner, the undersigned brought the examiner's new arguments in the office action of 01/09/04 to his attention. The examiner, after consulting with his supervisor, agreed that the final rejection was premature, and also agreed to remove the finality of the office action. Thereafter, a full amendment after final, highlighting the conversation, and including examiner's suggested amendments that would come under favorable view was drafted and filed on 2/25/04.

The supplemental final rejection of 3/22/2004 comes as a surprise, especially since a full and complete response by the applicants, removing any issues for rejection, was presented but not entered. It is noted that the applicants did not request a supplemental action, nor did they request the clock for the office action to be reset (MPEP 710.06), nor did the action cross the amendment (MPEP 714.05). Rather, applicants entered a full amendment in response to the action of 01/09/04. It is believed that the examiner did not follow proper procedure by refusal to enter the amendment, while issuing yet another final rejection.

On paragraph 2 of the office action, the examiner states that the after-final amendments filed 2/24/04 were not entered because they fail to comply with the requirements of form expressly set forth in a previous office action. Applicants respectfully disagree.

The first office action of 8/1/2003 provided a 35 USC 112, 2nd paragraph rejection for the use of the term RRP (paragraphs 6 and 7), and a 35 USC 112, 1st paragraph

enablement rejection because according to the examiner, while RRP 1-2, 4-8 and mouse RRP were enabled, all RRPs were not enabled (paragraph 8). The response of 10/27/2003 provided argument for the indefiniteness rejection, but noted that an examiner's amendment would be acceptable to applicants should the rejection be maintained (pages 6 and 7), and also amended the claims to satisfy the enablement requirement of 35 USC 112, 1st paragraph by naming the RRPs (pages 5 and 7).

The office action of 1/9/04 rejected the claims again for indefiniteness (paragraph 4), and introduced a 35 USC 112, 1st paragraph written description rejection (paragraph 5), stating "The guidelines for the examination of patent applications under the 35 U.S.C. ¶ 1 "Written Description" requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species ....(Federal Register, Vol 66, No.4, pages 1099-1111, Friday January 5, 2001, see especially page 1006 3rd column". The after final response of 2/25/2004 amended the claims to spell out RRP and also identified all sequences by their SEQ ID NOs, thus expressly following examiner's suggestion and requirement of form (pages 2-4). Thus, the amendment should have been entered.

In light of the withdrawal of the 1/9/04 rejection, the current office action reiterates the indefiniteness rejection (paragraph 5) and provides a 35 USC 112, 1st paragraph written description requirement rejection (paragraph 6). The indefiniteness rejection was already addressed in the 10/27/03 and 2/25/04 amendments as stated above, and should have been entered. The written description rejection also spells out the SEQ ID NOs for which the written description requirement is satisfied (paragraph 6, lines 6-8). Again, the amendment of 2/25/04 already addressed this requirement (pages 2-4), and should have been entered.

Thus, it is not understood exactly what requirement of form the applicants have not yet satisfied that resulted in the non-entry of the 2/25/04 amendment. Accordingly, applicants request for the entry of the 2/25/04 amendment.

Claim Rejections – 35 USC §112, 2nd Paragraph

On paragraph 5 of the office action, claims 8-12 were rejected under 35 USC 112, 2nd paragraph as being indefinite. Amended claim 8 of 2/25/04, provided as Appendix A

below, clearly defines the term RRP, and also defines each RRP by a SEQ ID NO, and thus, overcomes the rejection.

As such, claims 8-12 meet the requirements of 35 USC 112, 2nd paragraph.

Claim Rejections – 35 USC §112, 1st Paragraph

On paragraph 6 of the office action, claims 8-12 were rejected under 35 USC 112, first paragraph, for lack of proper written description for all RRPs in literature. Amended claim 8 of 2/25/04 amendment, also attached as Appendix A below, provides a clear definition of the term RRP, and further identifies each RRP using a SEQ ID NO, thus overcoming the rejection.

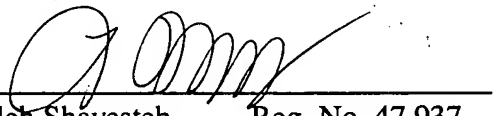
As such, claims 8-12 meet the written description requirement of 35 USC 112, 1st paragraph.

CONCLUSION

It is believed that all the objections and rejections raised by the Examiner have been addressed and that the application is in condition for allowance. The Examiner is encouraged to telephone the undersigned with any questions or comments regarding this response.

Respectfully submitted,

Dated: May 3, 2004



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(Customer No. 23500)

Appendix A - Claims as presented in the 02/25/2004 amendment

1-7. (Canceled)

8. (Currently amended) A method of screening for agents that modulate the interaction of ~~an~~ Rhomboid Related Protein (RRP) polypeptide with an RRP binding target, comprising:

a) expressing a recombinant RRP polypeptide,

b) incubating the recombinant RRP polypeptide with an RRP binding target and a candidate RRP modulating agent and

c) determining whether said candidate RRP modulating agent modulates the binding of RRP polypeptide with the RRP binding target,

wherein RRP is selected from the group consisting of SEQ ID NO:2 (RRP1), SEQ ID NO:4 (RRP2), SEQ ID NO:6 (RRP3), SEQ ID NO:8 (RRP4), SEQ ID NO:10 (RRP5), SEQ ID NO:12 (RRP6), SEQ ID NO:14(RRP7), SEQ ID NO:16 (RRP8), and SEQ ID NO:46 (mRRP1).

9. (Original claim) The method according to claim 8 wherein said binding target is selected from the group consisting of TGFα, EGF, and amphiregulin.

10. (Original claim) The method according to claim 8 wherein said binding target is TGFα.

11. (Original claim) The method according to claim 8 wherein said candidate RRP modulating agent is an antibody.

12. (Original claim) The method according to claim 8 wherein said candidate RRP modulating agent is a small organic molecule.

13-51. (Canceled).

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/056,790	01/23/2002	Mario N. Lioubin	EX02-004C	1603

23500 7590 03/22/2004

JAN P. BRUNELLE
EXELIXIS, INC.
170 HARBOR WAY
P.O. BOX 511
SOUTH SAN FRANCISCO, CA 94083-0511

EXAMINER	
YAEN, CHRISTOPHER H	
ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 03/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)	
10/056,790	LIOUBIN ET AL.	
Examiner	**Art Unit**	
Christopher H Yaen	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 October 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

SUPPLEMENTAL DETAILED ACTION

1. As noted by applicants, the Final Action mailed 01/09/2004 contained an apparent oversight wherein the Examiner presented new arguments under 35 USC 112 1st paragraph, in the absence of referring to MPEP 706.07(a). Thus, this office Action represents a subsequent action on the merits in **response** to the amendments filed October 27, 2003. The Action mailed 01/09/04 is therefore withdrawn in favor of this supplemental action.

2. The After-Final amendments filed 02/25/2004 will not be entered because they fail to comply with the requirements of form expressly set forth in a previous Office Action. 37 CFR 1.116(b).

3. Claims 1-7, and 13-51 are canceled without prejudice or disclaimer.

4. Claims 8-12 are pending and examined on the merits.

Claim Rejections Maintained - 35 USC § 112, 2nd paragraph

5. The rejection of claims 8-12 under 35 USC 112, 2nd paragraph as being indefinite is maintained for the reasons of record. Applicant argues that the specification provides clear indication the term "RRP" is intended to refer to a **R**homboid **R**elated **P**rotein. Moreover, applicant states that because the RRPs are characterized in the specification by sequence identification numbers, there is clear indication to one of skill in the art that RRP is intended to refer only to Rhomboid Related Proteins. Applicant's arguments have been carefully considered but are not found persuasive because others, as evidenced by Salvo *et al* and Barg *et al*, have also defined RRPs. Because the skilled

artisan cannot determine which "RRP" is intended to be encompassed with the scope of the claims, and because there are other names or meanings for the term "RRP", it is ambiguous and indefinite. As such, there is no clear distinction as to which RRP is being claimed by the applicant.

New Arguments

Claim Rejections - 35 USC § 112, 1st paragraph

6. Claims 8-12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The written description in this case has only set forth sequences represented by the sequences of SEQ ID Nos: 2,4,6,8,10,12,14,16 and 46, and is therefore the written description is not commensurate in scope to claims that read on RRPs 1-8 and mouse RRP.

In order to fulfill the requirements of written description, the specification as originally filed must convey to one of skill in the art that the applicant was in possession of the instantly claimed invention. As provided in the last office action, other have discovered or characterized RRP proteins such as Szakmary *et al* and Savino *et al* (previously cited), both of which specifically characterized a RRP1 protein. It does not appear that the specification has described a RRP protein with the same characteristics and as such is not entitled to the broad scope of RRPs, especially RRP-1. There has

been no structurally defined characteristics associated with the RRPs so that one of skill in the art would be able to practice the invention commensurate in scope to the claims. The Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 3rd column).

Applicant was not in possession of the instant claimed invention. See Regents of the University of California v. Eli Lilly and Co. 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). Adequate written description of genetic material "'requires a precise definition, such as by structure, formula, chemical name, or physical properties,' not a mere wish or plan for obtaining the claimed chemical invention." Id. 43 USPQ2d at 1404 (quoting Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606). The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter of the claim. Id. 43 USPQ2d at 1406. A description of what the genetic material does, rather than of what it is, does not suffice. Id.

While it is noted that the instant claims are drawn to methods, the claims nevertheless require an adequate written description of the "RRP(s)" employed in the methods.

Conclusion

7. No claim is allowed.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H Yaen whose telephone number is 571-272-0838. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 571-272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Christopher Yaen
Art Unit 1642
March 17, 2004

GARY NICKOL
PRIMARY EXAMINER

MODE = MEMORY TRANSMISSION START=FEB-25 11:48 END=FEB-25 11:50

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Reply to Final Rejection Under 37 C.F.R. § 1.116 with Amendment (4p)

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Reply to Final Rejection Under 37 C.F.R. § 1.116 with Amendment (4p)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of: Lioubin *et al.*	Confirmation No: 1603
Serial No.: 10/056,790	Group Art Unit: 1642
Filed: 1/23/2002	Examiner: Yaen, Christopher H.
For: RRP Sequences and Knockout Mice and Uses Thereof	Attorney Docket No: EX02-004C

REPLY TO FINAL REJECTION UNDER 37 C.F.R. § 1.116 WITH AMENDMENT

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Via Facsimile (703) 872-9306

Dear Commissioner:

This is responsive to the office action mailed 01/09/2004, making this a timely response. No fees are believed to be due at this time. However, if this belief is in error, the Commissioner is authorized to charge any fees required for consideration of this paper and any other papers filed herewith to deposit account number 50-1108.

AMENDMENTS TO THE CLAIMS

Please amend the claims to read as follows:

1-7. (Canceled)

8. (Currently amended) A method of screening for agents that modulate the interaction of ~~a~~ an Rhomboid Related Protein (RRP) polypeptide with an RRP binding target, comprising:

a) expressing a recombinant RRP polypeptide,

b) incubating the recombinant RRP polypeptide with an RRP binding target and a candidate RRP modulating agent and

c) determining whether said candidate RRP modulating agent modulates the binding of RRP polypeptide with the RRP binding target,

wherein RRP is selected from the group consisting of SEQ ID NO:2 (RRP1), SEQ ID NO:4 (RRP2), SEQ ID NO:6 (RRP3), SEQ ID NO:8 (RRP4), SEQ ID NO:10 (RRP5), SEQ ID NO:12 (RRP6), SEQ ID NO:14(RRP7), SEQ ID NO:16 (RRP8), and SEQ ID NO:46 (mRRP1).

9. (Original claim) The method according to claim 8 wherein said binding target is selected from the group consisting of TGFα, EGF, and amphiregulin.

10. (Original claim) The method according to claim 8 wherein said binding target is TGFα.

11. (Original claim) The method according to claim 8 wherein said candidate RRP modulating agent is an antibody.

12. (Original claim) The method according to claim 8 wherein said candidate RRP modulating agent is a small organic molecule.

13-51. (Canceled).

REMARKS

In reviewing the office actions for this application, applicants note that the first office action of 08/01/2003 rejected claims 8-12 based on 35 USC 112, 2nd paragraph (indefiniteness), and 35 USC 112, 1st paragraph, enablement. The current final rejection of 01/09/2004 maintains the 35 USC 112, 2nd paragraph (indefiniteness) rejection, and states that the 35 USC 112, 1st paragraph is also maintained. However, the 35 USC 112, 1st paragraph rejection raised by the examiner is a written description rejection, and not an enablement rejection. As this is the first time a written description rejection has been raised, applicants believe that a final rejection is premature (see 37 C.F.R. § 1.113, MPEP § 706.07 (c-d)), and thus request reconsideration and withdrawal of the finality of the office action.

In a telephone conversation with the examiner on February 19, 2004, the undersigned brought this matter to the examiner's attention, and the examiner kindly agreed to remove the finality of the office action issued on 01/09/2004.

Amendments

Claim 8 has been amended to indicate RRP as Rhomboid Related Protein, and to identify each RRP with a SEQ ID NO. Support for the amendment is found on page 4, paragraph [0011], and page 7, paragraph [0027].

The amendments to the claims do not introduce new matter.

The examiner has previously found the subject matter of the claims enabled in office action of 08/01/2003, paragraph 8.

In a telephone conversation with the undersigned on February 18, 2004, the examiner kindly indicated that he would bring the above claims under favorable consideration.

Claim Rejections – 35 USC §112, 2nd Paragraph

On paragraph 4 of the office action, claims 8-12 were rejected under 35 USC 112, 2nd paragraph as being indefinite. Amended claim 8 clearly defines the term RRP, and also defines each RRP by a SEQ ID NO, and thus, overcomes the rejection.

As such, claims 8-12 meet the requirements of 35 USC 112, 2nd paragraph.

Claim Rejections – 35 USC §112, 1st Paragraph

On paragraph 5 of the office action, claims 8-12 were rejected under 35 USC 112, first paragraph, for lack of proper written description for all RRPs in literature. Amended claim 8 provides a clear definition of the term RRP, and further identifies each RRP using a SEQ ID NO, thus overcoming the rejection.

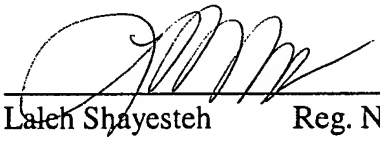
As such, claims 8-12 meet the written description requirement of 35 USC 112, 1st paragraph.

CONCLUSION

It is believed that all the objections and rejections raised by the Examiner have been addressed and that the application is in condition for allowance. The Examiner is encouraged to telephone the undersigned with any questions or comments regarding this response.

Respectfully submitted,

Dated: February 25, 2004



Laleh Shayesteh Reg. No. 47,937

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Reply to Final Rejection Under 37 C.F.R. § 1.116 with Amendment (4p)

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/056,790	01/23/2002	Mario N. Lioubin	EX02-004C	1603

23500 7590 01/09/2004

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EXAMINER	
YAEN, CHRISTOPHER H	
ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 01/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/056,790	LIOUBIN ET AL.	
	Examiner	Art Unit	
	Christopher H Yaen	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 October 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. The amendment filed 10/27/2003 is acknowledged and entered into the record.

2. Claims 1-7 and 13-51 are canceled.

3. Claims 8-12 are pending and examined on the merits.

Claim Rejections Maintained - 35 USC § 112, 2nd paragraph

4. The rejection of claims 8-12 under 35 USC 112, 2nd paragraph as being indefinite is maintained for the reasons of record. Applicant argues that the specification provides clear indication the term "RRP" is intended to refer to a **R**homboid **R**elated **P**rotein. Moreover, applicant states that because the RRPs are characterized in the specification by sequence identification numbers, the there is clear indication to one of skill in the art that RRP is intended to refer only to Rhomboid Related Proteins. Applicant's arguments have been carefully considered but are not found persuasive because others, as evidenced by Salvo *et al* and Barg *et al*, have also defined RRPs. Because the skilled artisan cannot determine which "RRP" is intended to be encompassed with the scope of the claims, and because there are other names or meanings for the term "RRP", it is ambiguous and indefinite. As such, there is no clear distinction as to which RRP is being claimed by the applicant.

Claim Rejections - 35 USC § 112, 1st paragraph

5. The rejection of claims 8-12 under 35 USC 112, 1st paragraph as lacking proper written description for all RRPs is maintained for the reasons of record. Applicant

argues that the amendment to the claims to refer specifically to RRP1-8 and mouse RRP1 overcomes the rejection of record. Applicant's arguments have been carefully considered but are not found persuasive. In order to fulfill the requirements of written description, the specification as originally filed must convey to one of skill in the art the applicant was in possession of the instantly claimed invention. As provided in the last office action, other have discovered or characterized RRP proteins such as Szakmary *et al* and Savino *et al*, both of which specifically characterized a RRP1 protein. It does not appear that the specification has described a RRP protein with the same characteristics and as such is not entitled to the broad scope of RRPs, especially RRP-1. There has been no structurally defined characteristics associated with the RRPs so that one of skill in the art would be able to practice the invention commensurate in scope to the claims. The Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 3rd column).

Applicant was not in possession of the instant claimed invention. See Regents of the University of California v. Eli Lilly and Co. 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). Adequate written description of genetic material "'requires a precise definition, such as by structure, formula, chemical name, or physical properties,' not a mere wish or plan for obtaining the claimed chemical invention." Id. 43 USPQ2d at 1404 (quoting Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606). The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter of the claim. Id. 43 USPQ2d at 1406. A description of what the genetic material does, rather than of what it is, does not suffice. Id.

Conclusion

6. **No claim is allowed.**

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H Yaen whose telephone number is 703-305-3586. The examiner can normally be reached on Monday-Friday 9-5. 571-272-0838

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone number for the organization where this application or proceeding is assigned is 703-308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Christopher Yaen
Art Unit 1642
December 20, 2003

CY

PTO/SB/97 (08-03)
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REPLY UNDER 37 C.F.R. § 1.111 WITH AMENDMENT (7 pgs)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of: Lioubin *et al.*	Confirmation No: 1603
Serial No.: 10/056,790	Group Art Unit: 1642
Filed: 01/23/2002	Examiner: Christopher H. Yaen
For: RRP Sequences and Knockout Mice and Uses Thereof	Attorney Docket No: EX02-004C

REPLY UNDER 37 C.F.R. § 1.111 WITH AMENDMENT

Commissioner for Patents
Alexandria, VA 22313-1450

Via Facsimile 703-872-9306 (TC1600)

Dear Commissioner:

This is responsive to the office action mailed 8/1/2003, making this a timely response. No fees are believed to be due at this time. However, if this belief is in error, the Commissioner is authorized to charge any fees required for consideration of this paper and any other papers filed herewith to deposit account number 50-1108.

AMENDMENTS TO THE SPECIFICATION

Please amend the specification to read as follows:

Paragraph [0029]:

The term "RRP polypeptide" refers to a full-length RRP protein or a functionally active fragment or derivative thereof. A "functionally active" RRP fragment or derivative exhibits one or more functional activities associated with a full-length, wild-type RRP protein, such as antigenic or immunogenic activity, enzymatic activity, ability to bind natural cellular substrates, etc. The functional activity of RRP proteins, derivatives and fragments can be assayed by various methods known to one skilled in the art (Current Protocols in Protein Science (1998) Coligan et al., eds., John Wiley & Sons, Inc., Somerset, New Jersey) and as further discussed below. For purposes herein, functionally active fragments also include those fragments that comprise one or more structural domains of an RRP, such as a protease or rhomboid domain or a binding domain. Catalytic and other domains can be identified using the PFAM program (Bateman A., et al., Nucleic Acids Res, 1999, 27:260-2~~; http://pfam.wustl.edu~~). Methods for obtaining RRP polypeptides are also further described below. Preferred fragments are functionally active, domain-containing fragments sharing at least 80% sequence identity or similarity, preferably at least 85%, more preferably at least 90%, and most preferably at least 95% sequence identity or similarity with a contiguous stretch of at least 25 amino acids, preferably at least 50 amino acids, more preferably at least 100 amino acids, and in some cases, the entire length of any one of SEQ ID NOs:2, 4, 6, 8, 10, 12, 14, 16, and 46. In further preferred embodiments, the fragment comprises the entire rhomboid domain (PFAM 01694).

Paragraph [0040]:

Preferably, the RRP polypeptide nucleic acid, fragment, ortholog, or derivative thereof has at least 70% sequence identity, preferably at least 80%, more preferably 85%, still more preferably 90%, and most preferably at least 95% sequence identity with RRP. Normally, orthologs in different species retain the same function, due to presence of one or more protein motifs and/or 3-dimensional structures. As used herein, "percent (%)

sequence identity" with respect to a subject sequence, or a specified portion of a subject sequence, is defined as the percentage of nucleotides or amino acids in the candidate derivative sequence identical with the nucleotides or amino acids in the subject sequence (or specified portion thereof), after aligning the sequences and introducing gaps, if necessary to achieve the maximum percent sequence identity, as generated by the program WU-BLAST-2.0a19 (Altschul *et al.*, J. Mol. Biol. (1997) 215:403-410; http://blast.wustl.edu/blast/README.html) with all the search parameters set to default values. The HSP S and HSP S2 parameters are dynamic values and are established by the program itself depending upon the composition of the particular sequence and composition of the particular database against which the sequence of interest is being searched. A % identity value is determined by the number of matching identical nucleotides or amino acids divided by the sequence length for which the percent identity is being reported. "Percent (%) amino acid sequence similarity" is determined by doing the same calculation as for determining % amino acid sequence identity, but including conservative amino acid substitutions in addition to identical amino acids in the computation.

Paragraph [00132]:

RNA was extracted from each tissue sample using Qiagen (Valencia, CA) RNeasy kits, following manufacturer's protocols, to a final concentration of 50ng/µl. Single stranded cDNA was then synthesized by reverse transcribing the RNA samples using random hexamers and 500ng of total RNA per reaction, following protocol 4304965 of Applied Biosystems (Foster City, CA, http://www.appliedbiosystems.com/).

Paragraph [0042]:

Alternatively, an alignment for nucleic acid sequences is provided by the local homology algorithm of Smith and Waterman (Smith and Waterman, 1981, Advances in Applied Mathematics 2:482-489; database: European Bioinformatics Institute wwwz.ebi.ac.uk/bic.sub.--sw/; Smith and Waterman, 1981, J. of Molec.Biol., 147:195-197; Nicholas et al., 1998, "A Tutorial on Searching Sequence Databases and Sequence Scoring Methods" (www.psc.edu) and references cited therein.; W.R.

Pearson, 1991, Genomics 11:635-650). This algorithm can be applied to amino acid sequences by using the scoring matrix developed by Dayhoff (Dayhoff: Atlas of Protein Sequences and Structure, M. O. Dayhoff ed., 5 suppl. 3:353-358, National Biomedical Research Foundation, Washington, D.C., USA), and normalized by Gribskov (Gribskov 1986 Nucl. Acids Res. 14(6):6745-6763). The Smith-Waterman algorithm is used to search databases for sequences similar to a query sequence. Smith-Waterman uses dynamic programming to determine how an optimal alignment between the query sequence and a database sequence can be produced. This alignment is obtained by determining what transformations the query sequence would need to undergo to match the database sequence. Transformations include substituting one character for another and inserting or deleting a string of characters. A score is assigned for each character-to-character comparison--positive scores for exact matches and some substitutions, negative scores for other substitutions and insertions/deletions. The first character in an insertion or deletion gap is scored with a gap open penalty and subsequent characters are scored with a gap extension penalty. Scores are obtained from statistically-derived scoring matrices. The combination of transformations that results in the highest score is used to generate an alignment between the query sequence and database sequence. Smith-Waterman algorithm may be employed where default parameters are used for scoring (for example, gap open penalty of 12, gap extension penalty of two). From the data generated the "Match" value reflects "sequence identity."

AMENDMENTS TO THE CLAIMS

Please amend the claims to read as follows:

1-7. (Canceled)

8. (Currently amended) A method of screening for agents that modulate the interaction of an RRP polypeptide with an RRP binding target, comprising:

a) expressing a recombinant RRP polypeptide,

b) incubating the recombinant RRP polypeptide with an RRP binding target and a candidate RRP modulating agent and

c) determining whether said candidate RRP modulating agent modulates the binding of RRP polypeptide with the RRP binding target,

wherein RRP is selected from the group consisting of RRP1, RRP2, RRP3, RRP4, RRP5, RRP6, RRP7, RRP8, and mRRP1,.

9. (Original claim) The method according to claim 8 wherein said binding target is selected from the group consisting of TGFα, EGF, and amphiregulin.

10. (Original claim) The method according to claim 8 wherein said binding target is TGFα.

11. (Original claim) The method according to claim 8 wherein said candidate RRP modulating agent is an antibody.

12. (Original claim) The method according to claim 8 wherein said candidate RRP modulating agent is a small organic molecule.

13-51. (Canceled).

REMARKS

Amendments

Specification has been amended to remove hyperlinks.

Claims have been amended to more particularly point out the claimed invention, as further described below. Support for amended claim 8 is found throughout the application, and in particular on paragraphs [0027] and [00146]. Claims 1-7 and 13-51 were canceled as they are drawn to non-elected subject matter.

The amendments to the specification or to the claims do not introduce new matter.

Objections to Specification

On paragraph 5 of the office action, the specification was objected to for containing embedded hyperlinks. Hyperlinks have been removed from the specification, and as such, the objection is overcome.

Claim Rejections – 35 USC § 112, 2nd paragraph

On paragraphs 6 and 7 of the office action, claims 8-12 were rejected under 35 USC 112, second paragraph for use of the term "RRP", for being unclear as to the metes and bounds of the term. Applicants respectfully disagree.

MPEP 2173.05(a) provides: "The meaning of every term used in a claim should be apparent from the prior art or from the specification and drawings at the time the application is filed". The term "RRP" has been clearly defined on paragraph [0011], as "Rhomboid Related Proteins", and meaning a mammalian ortholog of Drosophila Rhomboid, and more specifically, RRP1-RRP8, and mouse RRP1 (mRRP1). Further detail is provided on page 6, paragraph [0023]. The examiner provides Barg S et al publication describing RRP as a "readily releasable pool", and Savino TM et al publication describing RRP as "ribosomal RNA processing proteins". However, given the facts provided above, and since sequences of RRP proteins that can be used in the invention are clearly identified on pages 7 and 8, paragraph [0027] of the specification, there remains little doubt as to the meaning of "RRP" in the instant specification. As such, the use of the term "RRP" meets the requirements of 35 USC 112, second paragraph. However, if the examiner still does not find this argument persuasive, and to

further the prosecution, the examiner is authorized to recite the full name via an examiner's amendment.

Claim Rejections – 35 USC § 112, 1st paragraph

On paragraph 8 of the office action, claims 8-12 were rejected under 35 USC 112, 1st paragraph, for lack of reasonable enablement for all RRPs. Amended claim 8 refers to RRPs 1-8 and mouse RRP1 (mRRP1), and as such, overcomes the rejection.

On the same paragraph, the examiner kindly indicates the specification as enabling for an RRP1, 2, 4, 5, 6, 7, 8, and mRRP1. However, the examiner does not include RRP3 in his indication. This might be due to a misreading of the specification. The specification teaches the characterization of 9 different RRP polypeptides by sequence identification numbers. Specifically, paragraph [0027] provides RRP1 through 8 and mouse mRRP1 polypeptides, having SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14, 16, and 46, respectively. Thus, the specification is enabling for RRP 1 through 8, and mRRP1. Currently amended claim 8 reflects these polypeptides.

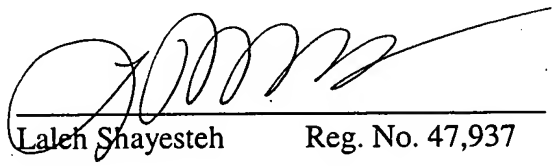
As such, claims 8-12 meet the requirements of 35 USC 112, 1st paragraph.

CONCLUSION

It is believed that all the objections and rejections raised by the Examiner have been addressed and that the application is in condition for allowance. The Examiner is encouraged to telephone the undersigned with any questions or comments regarding this response.

Respectfully submitted,

Dated: October 27, 2003



Laleh Shayesteh Reg. No. 47,937

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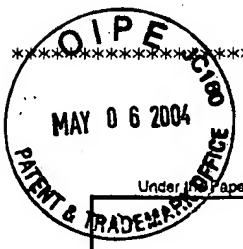

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REPLY UNDER 37 C.F.R. § 1.111 WITH AMENDMENT (7 pgs)

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/056,790	01/23/2002	Mario N. Lioubin	EX02-004C	1603

23500 7590 08/01/2003

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EXAMINER	
YAEN, CHRISTOPHER H	
ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 08/01/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)	
10/056,790	LIOUBIN ET AL.	
Examiner	**Art Unit**	
Christopher H Yaen	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-51* is/are pending in the application.

4a) Of the above claim(s) *1-7 and 13-51* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4&5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of group II in Paper No. 9 is acknowledged.

2. Claims 1-51 are pending, claims 1-7 and 13-51 are withdrawn from further consideration as being drawn to non-elected subject matter. Applicant is reminded to cancel claims drawn to inventions non-elected.

3. Therefore, claims 8-12 are examined on the record.

Information Disclosure Statement

4. The Information Disclosure Statements filed 5/17/02 & 3/25/02 (paper no. 4 & 5) are acknowledged and considered. A signed copy of the IDS is attached hereto.

Specification

5. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. See pages, 8,44 for example.

Claim Rejections - 35 USC § 112, 2nd paragraph

6. Claims 8-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. With regard to claims 8, 11, 12 and dependents thereof, in the recitation of the term "RRP", it is unclear as the metes and bounds of the term. Barg S *et al* (Neuron. 2002 Jan 17;33(2):287-99) disclose that RRP is "a readily releasable pool". Savino TM

et al (J Cell Sci. 1999 Jun;112 (Pt 12):1889-900) describe RRP1-RRP6 as ribosomal RNA processing proteins. Because the termed used in the instant invention can fall within the scope of "RRP" used by Barg S *et al* or Savino *et al*, the term is considered indefinite. This term is considered a laboratory term of which many possible meanings can be derived. Applicant is advised to amend the claim to recite the full name of the instantly claimed protein.

Claim Rejections - 35 USC § 112, 1st paragraph

8. Claims 8-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an RRP1-2, 4-8 and mouse RRP1 (mRRP1) having SEQ ID Nos: 36-44, and 46 does not reasonably provide enablement for all RRPs. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The claims of the instant invention are drawn to a method of screening for an agent that modulates that the interaction of an RRP polypeptide with an RRP binding target.

The specification specifically teaches the characterization of 8 different RRP polypeptides by sequence identification numbers (RRP1-2, 4-8, and mRRP1). However, the specification has not taught the scope of the proteins encompassed by the term RRP. Szakmary *et al* (PNAS USA 1996; 93:1607-1612) teach an RRP1 molecule that is involved in the repair of oxidative DNA damage. Savino *et al* teach another RRP1 protein that is involved in pre-rRNA processing from 27S to 25S and

5.8S. Therefore, given the fact that there are multiple forms of RRP proteins that seem to be involved in distinctly different functions, have different protein structures, the specification has not enabled ,methods of screening for any and all agents that may or may not modulate all forms of RRP. Because these RRPs seem to have different functionalities, the resulting endpoints disclosed by the method cannot be properly assessed to all forms of RRP. The disclosure of the instant specification has only enabled the assaying of RRPs and their involvement in the EGFR signal transduction pathway. As such one of skill in the art would be forced into undue experimentation to determine the distinct endpoints for agents that would modulate other RRPs encompassed by the claims of the instant invention.

Therefore, considering large quantity of experimentation needed, the state of the art, and the breadth of the claims, it is concluded that undue experimentation would be required to enable the intended claim. Many of these factors have been summarized *In re Wands, 858 F.2d 731, USPQ2d 1400 (Fed. Cir. 1988).*

Conclusion

No claims are allowed

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H Yaen whose telephone number is 703-305-3586. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-

308-4242 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Christopher Yaen
Art Unit 1642
July 25, 2003